```
      (FILE 'USPAT' ENTERED AT 11:15:06 ON 08 JUN 1998)
L1         90628 S NOTCH
L2           373 S L1(P)DELTA
L3             6 S L2(P)(PROLIFERAT? OR DIFFERENTIAT? OR CELL(W)FATE OR REG
ENE
                 E ARTAVANIS-TSAKONA/IN
L4           310 S E4:E5
L5             2 S L4 AND NOTCH
```

Set	Items	Description
S1	97115	NOTCH
S2	1083	S1(15N)DELTA
S3	230	S2(15N)(PROLIFERAT? OR DIFFERENTIAT? OR CELL(W)FATE OR CANCER OR REGENERAT?)
S4	78	RD (unique items)
S5	489	E1:E10, E16, E17
S6	326	S5 AND NOTCH
S7	88	S6 AND DELTA
S8	34	RD (unique items)

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4/7/41 (Item 41 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

10405480 BIOSIS Number: 96005480
IMPLICATIONS OF DYNAMIC PATTERNS OF DELTA AND NOTCH EXPRESSION FOR CELLULAR INTERACTIONS DURING DROSOPHILA DEVELOPMENT
KOOH P J; FEHON R G; MUSKAVITCH M A T
PROGRAM GENETICS, CELL DEV. BIOLOGY, DEP. BIOLOGY, INDIANA UNIV., BLOOMINGTON, INDIANA 47405, USA.
DEVELOPMENT (CAMB) 117 (2). 1993. 493-507. CODEN: DEVPE
Full Journal Title: DEVELOPMENT (Cambridge)
Language: ENGLISH
Delta and **Notch** function are required for **cell fate** specification in numerous tissues during embryonic and postembryonic Drosophila development. Delta is expressed by all members of interacting cell populations within which fates are being specified and is subsequently down-regulated as cells stably adopt particular fates. Multiphasic expression in the derivatives of many germ layers implies successive requirements for Delta function in a number of tissues. At the cellular level, Delta and Notch expression are generally coincident within developing tissues. At the subcellular level, Delta and Notch are localized in apparent endocytic vesicles during down-regulation from the surfaces of interacting cells, implying an interaction consistent with their proposed roles as signal and receptor in cellular interactions during development.

4/7/42 (Item 42 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

10110234 BIOSIS Number: 95110234
DLK A PUTATIVE MAMMALIAN HOMEOTIC GENE DIFFERENTIALLY EXPRESSED IN SMALL CELL LUNG CARCINOMA AND NEUROENDOCRINE TUMOR CELL LINE
LABORDA J; SAUSVILLE E A; HOFFMAN T; NOTARIO V
CENTER BIOL. RESEARCH, FDA., 8800 ROCKVILLE PIKE, BLDG. 29, BETHESDA, MD 20892, USA.
J BIOL CHEM 268 (6). 1993. 3817-3820. CODEN: JBCHA
Full Journal Title: Journal of Biological Chemistry
Language: ENGLISH
Gastrin releasing peptide is mitogenic for mouse Swiss 3T3 fibroblasts and certain human small cell lung carcinoma (SCLC) cells but not for mouse Balb/c 3T3 fibroblasts. To identify new molecules associated with the gastrin releasing peptide-responsive phenotype, clones isolated from a differential cDNA library between Swiss and Balb/c 3T3 fibroblasts were used to screen for their expression in human SCLC cell lines. Using this approach, we have isolated and characterized human and mouse cDNA clones encoding a novel protein. This protein is a putative transmembrane protein belonging to the epidermal growth factor-like superfamily. In vitro transcription and translation studies detect a 42-kDa protein, in agreement with the size predicted from the translated cDNA sequence. This protein (termed **Delta** -like or dlk) is highly homologous to invertebrate homeotic proteins, including **Delta**, and **Notch**, the products of neurogenic loci involved in normal neural **differentiation** in Drosophila. dlk is expressed in tumors with neuroendocrine features, such as neuroblastoma, pheochromocytoma, and a subset of SCLC cells lines. However, its expression in normal tissues is restricted to the adrenal gland and placenta. These data suggest that dlk may be involved in

neuroendocrine differentiation and, because of its cellular location and restricted expression in normal tissues, it may be a potential therapeutic target in neuroendocrine tumors, particularly SCLC.

4/7/44 (Item 44 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

7719734 BIOSIS Number: 90087734
LATERAL INHIBITION AND **CELL FATE** DURING NEUROGENESIS IN DROSOPHILA THE INTERACTIONS BETWEEN SCUTE **NOTCH** AND **DELTA**
CABRERA C V
MARIE CURIE RES. INST., THE CHART, OXTED, SURREY RH8 0TL, UK.
DEVELOPMENT (CAMB) 109 (3). 1990. 733-742. CODEN: DEVPE
Full Journal Title: DEVELOPMENT (Cambridge)
Language: ENGLISH
A comparison of the patterns of expression of AS-C (T3) RNA and protein suggests that an important level of regulation occurs post-transcriptionally. First, when the RNA is abundant in the early embryo the protein is barely detectable. Later, the protein starts to accumulate in only a subset of the nuclei of those cells expressing the RNA. Only the cells in the subsets become the neuroblasts. This post-transcriptional regulation is suppressed in embryos mutant for the genes Notch and Delta; where all cells expressing RNA accumulate protein. These findings suggest that deployment of T3 protein expression is one of the causal factors that assigns specific fates to the neuroblast and, in conseuence, a basis for the mechanism of lateral inhibition is proposed.

4/7/58 (Item 2 from file: 351)
DIALOG(R)File 351:DERWENT WPI

009271449
WPI Acc No: 92-398861/199248
Human Notch and Delta DNA and protein sequences - used for study and manipulation of differentiation processes
Patent Assignee: UNIV INDIANA FOUND (INDV); UNIV YALE (UYYA)
Inventor: ARTAVANIS-TSAKONAS S; BLAUMUELLER C M; FEHON R G; MUSKAVITCH M A T; REBAY I; SHEPARD S B; FEHON R; MUSKAVITCH M A; SHEPARD S
Number of Countries: 023 Number of Patents: 007
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9219734	A1	19921112	WO 92US3651	A	19920501	B	199248 B
AU 9219197	A	19921221	AU 9219197	A	19920501	B	199311
			WO 92US3651	A	19920501		
EP 576623	A1	19940105	EP 92911557	A	19920501	B	199402
			WO 92US3651	A	19920501		
JP 7503123	W	19950406	JP 92510668	A	19920501	B	199522
			WO 92US3651	A	19920501		
EP 576623	A4	19950118	EP 92911557	A	19920000	B	199545
AU 675203	B	19970130	AU 9219197	A	19920501	B	199713
US 5648464	A	19970715	US 91695189	A	19910503	B	199734
			US 94264534	A	19940623		

Priority Applications (No Type Date): US 91791923 A 19911114; US 91695189 A 19910503; US 94264534 A 19940623
Cited Patents: 3.Jnl.Ref
Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
WO 9219734	A1	E	239			
Designated States (National): AU BR CA FI JP KR NO						
Designated States (Regional): AT BE CH DE DK ES FR GB GR IT LU MC NL SE						
AU 9219197	A			Based on		WO 9219734
EP 576623	A1	E		Based on		WO 9219734
Designated States (Regional): AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE						
JP 7503123	W			Based on		WO 9219734
AU 675203	B			Previous Publ.		AU 9219197
				Based on		WO 9219734
US 5648464	A		116	Cont of	US 91695189	

Abstract (Basic): WO 9219734 A

A purified human Notch protein and fragments are new. Also claimed are (1) chimeric proteins comprising fragments of the human Notch protein joined to a heterologous protein sequence, (2) derivs. or analogues of the human Notch protein characterised by the ability in vitro, when expressed on the surface of a first cell, to bind to a Delta protein expressed on the surface of a second cell, (3) a pure fragment of Drosophila Notch protein comprising of the epidermal growth factor (EGF)-like repeats 11 and 12 of the protein, (4) a pure fragment of a Delta protein characterised by the ability in vitro when expressed on the surface of a first cell to bind a Notch protein expressed on the surface of a second cell, (5) a chimeric protein comprising fragments of the Delta protein joined to a heterologous protein sequence, (6) a pure fragment of Delta protein which is characterised by the ability in vitro when expressed on the surface of a first cell to bind a second

Delta protein or fragment expressed on the surface of a second cell, (7) a pure fragment of the Serrate protein, which is characterised by the ability in vitro, when expressed on the surface of a first cell to bind to a Notch protein expressed on the surface of a second cell, (8) DNA (I) encoding a human Notch protein, or complementary to it, (9) a vector comprising (I), (10) a recombinant cell contg. the vector of (9), (11) an antibody which binds to human Notch protein but does not bind the Drosophila Notch protein and (12) DNA encoding (a) a protein sequence homologous to both a Serrate protein and a Delta protein and (b) a second amino acid sequence which is not homologous to either a Serrate protein or a Delta protein.

USE - The nucleic acid and amino acid and antibodies can be used for the detection and quantitation of mRNA for human **Notch** and **Delta** and adhesive molecules, to study its expression, to produce human **Notch** and **Delta** and adhesive sequences, for the study and manipulation of **differentiation** processes.

(Dwg.0/25

Abstract (Equivalent): US 5648464 A

A novel substantially purified protein comprises an amino acid sequence encoded by the 267, 574, or 295 nucleotide DNA sequences given in the specification, which is able to be bound by an antibody to a human Notch protein but not to a Notch protein of another species.

Dwg.0/24

Derwent Class: B04; D16

International Patent Class (Main): C07K-014/435; C12N-015/12; C12P-021/02

International Patent Class (Additional): C07K-007/10; C07K-013/00; C07K-014/47; C07K-015/12; C12N-005/10; C12N-015/63; C12P-021/00;

4/7/60 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

143356 DBA Accession No.: 93-01408 PATENT
Human, Drosophila and Xenopus chimeric Notch protein and Delta protein and Serrate protein expression - for use in manipulation of differentiation; toporythmic gene DNA sequence
PATENT ASSIGNEE: Yale-Univ.; Indiana-Univ.Found. 1992
PATENT NUMBER: WO 9219734 PATENT DATE: 921112 WPI ACCESSION NO.: 92-398861 (9248)
PRIORITY APPLIC. NO.: US 791923 APPLIC. DATE: 911114
NATIONAL APPLIC. NO.: WO 92US3651 APPLIC. DATE: 920501
LANGUAGE: English
ABSTRACT: The following are new: (1) chimeric proteins comprising fragments of purified human Notch protein (HNP) joined to a heterologous protein sequence (PS); (2) derivatives or analogs of the HNP able (in vitro) to bind to a Delta protein (DP) expressed on the surface of a second cell; (3) a pure fragment of Drosophila Notch protein (DNP) (or a Xenopus Notch protein) comprising the epidermal growth factor-like repeats 11 and 12 of the protein; (4) a pure fragment of a DP able to bind to a Notch protein expressed on the surface of a cell; (5) a chimeric protein comprising fragments of the DP joined to a heterologous PS; (6) a pure fragment of DP able to bind to a DP or fragment expressed on the surface of a cell; (7) a pure fragment of a Serrate protein able (in vitro) to bind to a Notch protein expressed on the surface of a cell; (8) DNA (I) encoding HNP, or complementary to it; (9) a vector comprising (I); (10) a recombinant cell containing (9); (11) an antibody binding to HNP but not binding to the DNP; and (12) DNA encoding a PS homologous to both a Serrate protein and a Delta protein, and a second PS not homologous to either a Serrate or Delta protein.

4/7/65 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

111091521 CA: 111(11)91521v JOURNAL
Molecular genetics of Delta, a locus required for ectodermal differentiation in Drosophila
AUTHOR(S): Alton, Althea K.; Fechtel, Kim; Kopczynski, Casey C.; Shepard, Scott B.; Kooh, Pamela J.; Muskavitch, Marc A. T.
LOCATION: Dep. Biol., Indiana Univ., Bloomington, IN, 47405, USA
JOURNAL: Dev. Genet. (N. Y.) DATE: 1989 VOLUME: 10 NUMBER: 3 PAGES: 261-72 CODEN: DGNTDW ISSN: 0192-253X LANGUAGE: English
SECTION:
CA203003 Biochemical Genetics
CA212XXX Nonmammalian Biochemistry
IDENTIFIERS: Drosophila gene Delta mol genetics, mutation Notch Delta Enhancer of split, phenotype interaction Notch Delta Espl development, ectoderm differentiation neurogenic gene Drosophila
DESCRIPTORS:
Embryo,ectoderm...
differentiation of, of Drosophila melanogaster, role of neurogenic gene product in
Gene and Genetic element,animal, Notch...
for neurogenic protein, of Drosophila melanogaster, effect of gene dosage on female wing phenotypes and interaction with Dl and E(spl) loci in relation to
Gene and Genetic element,animal, Enhancer of split...
for neurogenic protein, of Drosophila melanogaster, interaction with gene Dl and N proteins of
Gene and Genetic element,animal, Delta...
for neurogenic transcripts involved in ectodermal differentiation, of Drosophila melanogaster, mol. genetics of, interaction with Notch and E (spl) loci in relation to
Development,nonmammalian...
gene Delta expression during, of D. melanogaster, multiple transcripts and interaction with gene Notch and E(spl) products of
Mutation...
in Delta locus of Drosophila melanogaster, definition of multifunctional locus by, interallelic complementation in relation to
Complementation,genetic, interallelic...
in Delta locus of Drosophila melanogaster, mol. genetics of
Drosophila melanogaster...
neurogenic loci Dl and E(spl) and N of, interaction of products of
Protein sequences...
of homologous regions in blood-coagulation factor IX and Drosophila Delta DlZM protein
CAS REGISTRY NUMBERS:
9001-28-9 62229-50-9 Delta gene protein DlZM of Drosophila melanogaster homol. to

4/7/73 (Item 8 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci

12599071 Genuine Article#: LZ432 Number of References: 39
Title: THE PLEIOTROPIC FUNCTION OF DELTA DURING POSTEMBRYONIC DEVELOPMENT OF DROSOPHILA-MELANOGASTER
Author(s): PARODY TR; MUSKAVITCH MAT
Corporate Source: INDIANA UNIV,DEPT BIOL,PROGRAM GENET CELL & DEVBIOL/BLOOMINGTON//IN/47405; INDIANA UNIV,DEPT BIOL,PROGRAM GENET CELL & DEVBIOL/BLOOMINGTON//IN/47405
Journal: GENETICS, 1993, V135, N2 (OCT), P527-539
ISSN: 0016-6731
Language: ENGLISH Document Type: ARTICLE
Abstract: Analysis of the development of Delta (Dl) temperature-sensitive mutants pulsed at restrictive temperature during larval and pupal stages reveals multiple phenocritical periods during which reduction of Dl function affects viability and development of adult structures. Dl function is required during the third larval instar for post-pupal viability and during the first day of pupal development for viability through eclosion. Dl function is required biphasically for the development of sensory bristles. Earlier pulses lead to bristle multiplication and later pulses lead to bristle loss. The exact intervals during which multiplication and loss are induced vary for different bristles. Dl function is also required for development of most, if not all, cell types in the retina. Different pulses result in reduction in eye size, scarring, and glossiness, as well as multiplication and loss of interommatidial bristles. We also define intervals during which Dl function is required for aspects of leg and wing development. Phenocritical periods for Dl function are temporally coincident with those previously reported for Notch (N), consistent with the hypothesis that the proteins encoded by Dl and N interact throughout development to assure correct specification of cell fates in a variety of imaginal tissues.

4/7/74 (Item 9 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci

12370727 Genuine Article#: LF042 Number of References: 40
Title: DELTA-FUNCTION IS REQUIRED FOR BRISTLE ORGAN DETERMINATION AND MORPHOGENESIS IN DROSOPHILA
Author(s): PARKS AL; MUSKAVITCH MAT
Corporate Source: INDIANA UNIV,DEPT BIOL,PROGRAM GENET CELL & DEVBIOL/BLOOMINGTON//IN/47405
Journal: DEVELOPMENTAL BIOLOGY, 1993, V157, N2 (JUN), P484-496
ISSN: 0012-1606
Language: ENGLISH Document Type: ARTICLE

4/7/75 (Item 10 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci

12275334 Genuine Article#: KZ423 Number of References: 44
Title: MOUSE NOTCH - EXPRESSION IN HAIR-FOLLICLES CORRELATES WITH CELL FATE DETERMINATION

Author(s): KOPAN R; WEINTRAUB H
Corporate Source: FR[redacted]HUTCHINSON CANC RES CTR/SEATTL[redacted]WA/98104
Journal: JOURNAL OF CELL BIOLOGY, 1993, V121, N3 (MAY), P631-641
ISSN: 0021-9525
Language: ENGLISH Document Type: ARTICLE
Abstract: Many vertebrate tissues, including skin, are known to develop as a consequence of epithelial-mesenchymal interactions. Much less is known about the role of cell-cell interaction within the epithelial or the mesenchymal compartments in morphogenesis. To investigate cell-cell interactions during skin development, and the potential role of the Notch homolog in this process, we cloned the mouse homolog of Notch (mNotch) and studied its expression pattern, starting as early as mesoderm formation. The novel application of double-labeled in situ hybridization in vertebrates allowed high resolution analysis to follow the fate of mNotch expressing cells directly. In comparison with the distribution of Id mRNA, analysis confirmed that in the hair follicle high levels of mNotch are expressed exclusively in the epithelial compartment. Hair follicle matrix cells start expressing mNotch as different cell types become distinguishable in the developing follicle. mNotch mRNA expression persists throughout the growth phase of the follicle and maintains the same expression profile in the second hair cycle. The cells in the follicle that undergo a phase of high level mNotch expression are in transition from mitotic precursors to several discreet, differentiating cell types. Our observations point out that both in time (during development) and in space (by being removed one cell layer from the dermal papilla) mNotch expression is clearly separated from the inductive interactions. This is a novel finding and suggests that mNotch is important for follicular differentiation and possibly cell fate selection within the follicle.

4/7/76 (Item 11 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci

12270439 Genuine Article#: KY548 Number of References: 55
Title: ALTERED EPIDERMAL GROWTH FACTOR-LIKE SEQUENCES PROVIDE EVIDENCE FOR A ROLE OF NOTCH AS A RECEPTOR IN CELL FATE DECISIONS
Author(s): HEITZLER P; SIMPSON P
Corporate Source: FAC MED STRASBOURG,CNRS,GENET MOLEC EUCARYOTES LAB,INSERM/F-67085 STRASBOURG//FRANCE/; FAC MED STRASBOURG,CNRS,GENET MOLEC EUCARYOTES LAB,INSERM/F-67085 STRASBOURG//FRANCE/
Journal: DEVELOPMENT, 1993, V117, N3 (MAR), P1113-1123
ISSN: 0950-1991
Language: ENGLISH Document Type: ARTICLE
Abstract: In Drosophila each neural precursor is chosen from a group of cells through cell interactions mediated by Notch and Delta which may function as receptor and ligand (signal), respectively, in a lateral signalling pathway. The cells of a group are equipotential and express both Notch and Delta. Hyperactive mutant Notch molecules, (Abruptex), probably have an enhanced affinity for the ligand. When adjacent to wild-type cells, cells bearing the Abruptex proteins are unable to produce the signal. It is suggested that in addition to the binding of Notch molecules on one cell to the Delta molecules of opposing cells, the Notch and Delta proteins on the surface of the same cell may interact. Binding between a cell's own Notch and Delta molecules would alter the availability of these proteins to interact with their counterparts on adjacent cells.

4/7/77 (Item 12 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci

12191586 Genuine Article#: KT999 Number of References: 43

Title: COMPLEX FUNCTION AND EXPRESSION OF DELTA DURING DROSOPHILA OOGENESIS
Author(s): BENDER LP [redacted] OOH PJ; MUSKAVITCH MAT [redacted]
Corporate Source: INDIANA UNIV,DEPT BIOL,GENET CELL & DEV BIOL PROGRAM/BLOOMINGTON//IN/47405; INDIANA UNIV,DEPT BIOL,GENET CELL & DEV BIOL PROGRAM/BLOOMINGTON//IN/47405
Journal: GENETICS, 1993, V133, N4 (APR), P967-978
ISSN: 0016-6731
Language: ENGLISH Document Type: ARTICLE
Abstract: Delta (Dl) encodes a cell surface protein that mediates cell-cell interactions central to the specification of a variety of cell fates during embryonic and postembryonic development of Drosophila melanogaster. We find that the Delta protein is expressed intermittently in follicle cells and in germ-line cells during stages 1-10 of oogenesis. Furthermore, Delta expression during oogenesis can be correlated with a number of morphogenetic defects associated with sterility observed in Dl mutant females, including failure of stalk formation within the germarium and subsequent fusion of egg chambers, necrosis in germ-line cells, and multiphasic embryonic arrest of fertilized eggs. We have also identified a Dl mutation that leads to context-dependent defects in Dl function during oogenesis. Direct comparison of Delta protein expression with that of the Notch protein in the ovary reveals substantial, but incomplete, coincidence of expression patterns in space and time. We discuss possible roles for the Delta protein in cell-cell interactions required for cell fate specification processes during oogenesis in light of available developmental and histochemical data.

9/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

13783785 BIOSIS Number: 99783785
Secreted forms of **DELTA** and SERRATE define antagonists of **Notch** signaling in Drosophila
Sun X; **Artavanis-Tsakonas S**
Howard Hughes Med. Inst., Dep. Cell Biology Biol., Boyer Cent. Molecular Med., Yale Univ., New Haven, CT 06536-0812, USA
Development (Cambridge) 124 (17). 1997. 3439-3448.
Full Journal Title: Development (Cambridge)
ISSN: 0950-1991
Language: ENGLISH
Print Number: Biological Abstracts Vol. 104 Iss. 010 Ref. 141389
We examined the function of secreted forms of the two known Drosophila **Notch** ligands, **DELTA** and SERRATE, by expressing them under various promoters in the Drosophila developing eye and wing. The phenotypes associated with the expression of secreted **Delta** (DIS) or secreted Serrate (SerS) forms mimic loss-of-function mutations in the **Notch** pathway. Both genetic interactions between DIS or SerS transgenics and duplications or loss-of-function mutations of **Delta** or Serrate indicate that DIS and SerS behave as dominant negative mutations. These observations were extended to the molecular level by demonstrating that the expression of Enhancer of split m-**delta**, a target of **Notch** signaling, is down-regulated by SERS. The antagonistic nature of the two mutant secreted ligand forms in the eye is consistent with their behavior in the wing, where they are capable of down-regulating wing margin specific genes opposite to the effects of the endogenous ligands. This analysis uncovers secreted molecular antagonists of **Notch** signaling and provides evidence of qualitative differences in the actions of the two

9/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

8094782 BIOSIS Number: 91015782
DELTEX A LOCUS INTERACTING WITH THE NEUROGENIC GENES **NOTCH** **DELTA** AND MASTERMIND IN DROSOPHILA-MELANOGASTER
XU T; **ARTAVANIS-TSAKONAS S**
HOWARD HUGHES MEDICAL INST., DEP. CELL BIOL., YALE UNIVERSITY, NEW HAVEN, CONN. 06511.
GENETICS 126 (3). 1990. 665-678. CODEN: GENTA
Full Journal Title: Genetics
Language: ENGLISH
The **Notch** locus of Drosophila melanogaster, which codes for a transmembrane protein sharing homology with the mammalian epidermal growth factor, is one of a small number of zygotically acting genes, the so called neurogenic loci, which are necessary for the correct segregation of neural from epidermal lineages during embryogenesis. In an attempt to identify genes whose products may interact with that of **Notch**, we designed a genetic screen aimed at identifying suppressors of certain **Notch** mutations which are known to affect the extracellular epidermal growth factor homologous domain of **Notch**. Mutations in two neurogenic loci were identified as suppressors: **Delta**, whose product was recently shown to interact with **Notch** and mastermind. In addition, a third, X-linked gene was shown capable of acting as a suppressor. We show that this gene is the deltex locus, characterize the phenotype of deltex mutations, and demonstrate both a maternal an zygotic action of the locus. All deltex alleles behave as recessive viables affecting wing, ocellar and eye morphology. There are allele specific interactions between deltex and various **Notch** alleles; for example, deltex mutants with a reduced dosage of wild-type **Notch** die as pupae. deltex also interacts with **Delta** and mastermind in a fashion that is formally analogous to its interaction with **Notch** . These results emphasize the special relationship between **Notch**, **Delta** and mastermind suggested by previous work and indicate that deltex is likely to play an important role in the same genetic circuitry within which these three neurogenic loci operate.

9/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

7660029 BIOSIS Number: 90028029
MOLECULAR INTERACTIONS BETWEEN THE PROTEIN PRODUCTS OF THE NEUROGENIC LOCI **NOTCH** AND **DELTA** TWO EGF-HOMOLOGOUS GENES IN DROSOPHILA
FEHON R G; KOOH P J; REBAY I; REGAN C L; XU T; MUSKAVITCH M A T; **ARTAVANIS-TSAKONAS S**
HOWARD HUGHES MED. INST., DEP. CELL BIOL., YALE UNIV., NEW HAVEN, CT 06511.
CELL 61 (3). 1990. 523-534. CODEN: CELLB
Full Journal Title: Cell
Language: ENGLISH
Genetic analyses have raised the possibility of interactions between the gene products of the neurogenic loci **Notch** and **Delta**, each of which encodes a transmembrane protein and EGF homology. To examine the possibility of intermolecular association between the products of these two genes, we studied the effects of their expression on aggregation in Drosophila S2 cells. We find that **Notch**-expressing cells form mixed

aggregates specifically with cells that express **Delta** and that this process is calcium dependent. In addition, we show that **Notch** and **Delta** can associate within the membrane of a single cell, and further, that they form detergent-soluble intermolecular complexes. Our analyses suggest that **Notch** and **Delta** proteins interact at the cell surface via their extracellular domains.

9/7/20 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

011122234
WPI Acc No: 97-100159/199709
New vertebrate **Delta** protein, DNA and antibodies - for treating and preventing cancer, nervous system disorders and for tissue regeneration
Patent Assignee: IMPERIAL CANCER RES TECHNOLOGY (IMCR); UNIV YALE (UYYA)
Inventor: **ARTAVANIS-TSAKONAS S**; GRAY G E; HENRIQUE D M P; ISH-HOROWICZ D; LEWIS J H; HENRIQUE D; LEWIS J
Number of Countries: 021 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9701571	A1	19970116	WO 96US11178	A	19960628	C07H-017/00	199709 B
AU 9664817	A	19970130	AU 9664817	A	19960628	C07H-017/00	199720

Priority Applications (No Type Date): US 95589 A 19950628
Cited Patents: 3.Jnl.Ref
Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
WO 9701571	A1	E	135			
	Designated States (National): AU CA JP US					
	Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
AU 9664817	A			Based on		WO 9701571

Abstract (Basic): WO 9701571 A

A purified vertebrate **Delta** protein (A) and functional analogues, derivs. and fragments are new. Also claimed are: (1) a fragment of (A) which is able to display one or more functional activities of human **Delta** protein; (2) a chimeric protein comprising a fragment of (A) of at least 20 amino acids fused via a covalent bond to a second protein, which is different to (A); (3) an antibody (Ab) which binds to (A) but does not bind to a Drosophila **Delta** protein; and (4) an isolated nucleic acid (I) encoding (A) or a fragment, or nucleic acid complementary to (I).

USE - (A), (I), Abs and mols. containing these are used therapeutically in compsns. to treat or prevent diseases or disorders, such as a malignancy characterised by increased **Notch** activity or expression, or cervical, breast, lung or colon cancer, melanoma or seminoma (claimed). (A) may also be used to treat a nervous system disorder or to promote tissue regeneration. The oligonucleotide inhibits the expression of (A) in a cell. (A) may be used to diagnose a disease or disorder by measuring the binding ability of a **Notch** protein to bind to (A), or by measuring the level of (A) in a patient relative to a normal person.. The Abs can be used to detect and quantitate (A) mRNA and protein.

Dwg.0/14

Derwent Class: B04; D16
International Patent Class (Main): C07H-017/00
International Patent Class (Additional): C07K-014/00; C12N-005/00; C12N-015/00; C12P-021/06

9/7/23 (Item 1 from file: 358)
DIALOG(R)File 358:Current BioTech Abs
Royal Soc Chem & DECHEMA . All rts. reserv.

059550 CBA Acc. No.: 12-02-001238 DOC. TYPE: Patent
Binding domains in **Notch** and **Delta** proteins.
AUTHOR: **Artavanis-Tsakonas**, **S**.; Muskavitch, M. A. T.; Fehon, R. G.; Blaumueller, C. M.; Shepard, S. B.
CORPORATE SOURCE: Yale Univ.; Indiana Univ. Foundation, New Haven, CT 06511; Bloomington, IN 47402, USA; USA
CODEN: PIXXD2
PATENT NUMBER: WO 9219734
PATENT APPLICATION: US 695189 (910503)
PUBLICATION DATE: 12 Nov 1992 (921112) LANGUAGE: English
ABSTRACT: Nucleotide sequences of the human **Notch** and **Delta** genes are provided as are amino acid sequences of their encoded proteins, or fragments thereof containing an antigenic determinant or which are functionally active. Adhesive fragments and sequences thereof are also provided as are proteins ("toporythmic proteins") encoded by toporythmic genes which mediate homotypic or heterotypic binding to toporythmic proteins. The toporythmic genes refer to the genes **Notch**, **Delta**, and Serrate, as well as to other members of the **Delta**/Serrate family. Antibodies to human **Notch** and to adhesive fragments are also given.

9/7/26 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

121026887 CA: 121(3)26887m PATENT
Therapeutic and diagnostic methods and compositions based on Notch proteins and nucleic acids
INVENTOR(AUTHOR): Artavanis-Tsakonas, Spyridon; Fehon, Richard Grant; Zagouras, Panayiotis; Blaumueller, Christine Marie
LOCATION: USA
ASSIGNEE: Yale University
PATENT: PCT International ; WO 9407474 A1 DATE: 940414
APPLICATION: WO 93US9338 (930930) *US 955012 (920930) *US 83590 (930625)
PAGES: 232 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-031/00A; A61K-031/70B; A61K-037/02B; A61K-039/44B; A61K-039/395B; C07H-021/04B; G01N-033/53B; G01N-033/68B DESIGNATED COUNTRIES: AU; BB; BG; BR; BY; CA; CZ; FI; HU; JP; KR; KZ; LK; LV; MG; MN; MW; NO; NZ; PL; RO; RU; SD; SK; UA; US; UZ; VN DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT ; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA201006 Pharmacology
CA209XXX Biochemical Methods
IDENTIFIERS: human Notch protein therapeutic, cDNA antibody human Notch
DESCRIPTORS:
Gene,animal...
cDNA, for human Notch protein and Drosophila Delta protein
Deoxyribonucleic acid sequences,complementary...
for human Notch protein and Drosophila Delta protein
Alopecia... Cirrhosis... Intestine,neoplasm, colon, inhibitors... Keloid... Lung,neoplasm, inhibitors... Mammary gland,neoplasm, inhibitors... Neoplasm inhibitors,colon... Neoplasm inhibitors,lung... Neoplasm inhibitors,mammary gland... Neoplasm inhibitors,melanoma... Psoriasis...
Notch protein as diagnosistics and
Proteins,specific or class, gene Delta...
Notch protein as therapeutics in relation to
Deoxyribonucleic acids,complementary, antisense...
of human Notch gene, for diagnostics and therapeutics
Protein sequences...
of human Notch protein and Drosophila Delta protein
Gene,animal, Serrate...
protein of, Notch protein as therapeutics in relation to
Antibodies... Antibodies,monoclonal...
to human Notch protein, for diagnostics and therapeutics
Testis,neoplasm, seminoma... Uterus,neoplasm, cervix...
treatment and diagnosis of, Notch protein as diagnosistics and
CAS REGISTRY NUMBERS:
146636-21-7 amino acid sequence of
156067-46-8 156067-47-9 156067-48-0 156067-49-1 156067-50-4
156067-51-5 amino acid sequence of, therapeutics contg.
146636-19-3 human Notch protein homologous to, as therapeutics
148513-28-4 156067-52-6 156067-53-7 156067-54-8 156067-55-9 nucleotide sequence of
146636-08-0 146636-13-7 156067-43-5 156067-44-6 156067-45-7 nucleotide

9/7/28 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

118163654 CA: 118(17)163654k PATENT
Binding domains in Notch and Delta proteins involved in their mutual interaction
INVENTOR(AUTHOR): Artavanis-Tsakonas, Spyridon; Muskavitch, Marc Alan Telander; Fehon, Richard Grant; Rebay, Ilaria; Blaumueller, Christine Marie ; Shepard, Scott Brockewell
LOCATION: USA
ASSIGNEE: Yale University; Indiana University Foundation
PATENT: PCT International ; WO 9219734 A1 DATE: 921112
APPLICATION: WO 92US3651 (920501) *US 695189 (910503) *US 791923 (911114)
PAGES: 239 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/12A; C12N-015/63B; C12P-021/00B; C07K-013/00B DESIGNATED COUNTRIES: AU; BR; CA; FI; JP; KR; NO DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT ; LU; MC; NL; SE
SECTION:
CA206003 General Biochemistry
CA212XXX Nonmammalian Biochemistry
CA213XXX Mammalian Biochemistry
IDENTIFIERS: Notch Delta protein interaction Drosophila
DESCRIPTORS:
Gene,animal...
cDNA, for Notch and Delta proteins of human, cloning and expression of
Glycoproteins,specific or class, gene Notch, fusion products...
chimeric gene for, expression in animal cell culture of, interaction with Delta protein in relation to
Animal cell line,S2...
expression in, of cDNAs for Notch and Delta proteins, interaction of proteins in relation to
Deoxyribonucleic acid sequences,complementary...
for Notch and Delta proteins of Drosophila and human and Serrate protein of Drosophila
Proteins,specific or class, gene Delta...
fusion products, chimeric gene for, expression in animal cell culture of, interaction with Notch protein in relation to
Plasmid and Episome...
hN3k, cDNA for human Notch protein on, cloning in Escherichia coli of
Plasmid and Episome...
hN4k, cDNA for human Notch protein on, cloning in Escherichia coli of
Plasmid and Episome...
hN5k, cDNA for human Notch protein on, cloning in Escherichia coli of
Adhesion,bio-...
induction of, by expression of Notch and Delta genes
Glycoproteins,specific or class, gene Notch...
interaction with Delta protein of and cloning of cDNA for human homolog of
Proteins,specific or class, gene Serrate...
interaction with Delta protein of, identification of domains involved in
Proteins,specific or class, gene .delta....
interaction with Notch protein of and cloning of cDNA for human homolog of
Gene,animal, Notch...
of Drosophila, expression in animal cell culture of, identification of Delta interacting domains in
Gene,animal, Delta...

of Drosophila, expression in animal cell culture of, identification of Notch interacting domains in
Protein sequences...
of Notch and Delta and Serrate proteins of Drosophila
Plasmid and Episome...
pMTD11, Delta protein cDNA on, expression in S2 cells of
Plasmid and Episome...
pMtNMg, Notch protein cDNA on, expression in S2 cells of
Antibodies...
to Notch and Delta and Serrate proteins of Drosophila
CAS REGISTRY NUMBERS:
146636-25-1 amino acid sequence of
146636-19-3 amino acid sequence of and role in interaction with Delta protein of
146636-21-7 amino acid sequence of, complete, and expression in cell culture of cDNA for
146636-26-2 amino acid sequence of, in interaction with Delta and Notch proteins
7440-70-2 biological studies, in interaction of Notch and Delta proteins
146636-22-8 in interaction with Notch and Serrate proteins
146636-06-8 146636-07-9 146636-08-0 146636-09-1 146636-10-4 146636-11-5 146636-12-6 146636-13-7 146636-14-8 146636-15-9 146636-16-0 146636-17-1 146636-18-2 nucleotide sequence and cloning in Escherichia coli of
140085-10-5 146636-23-9 146636-24-0 nucleotide sequence of
146636-20-6 nucleotide sequence of, complete, and expression in cell culture of

9/7/30 (Item 2 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci

11183268 Genuine Article#: GN927 Number of References: 45
Title: CHOOSING A CELL FATE - A VIEW FROM THE **NOTCH** LOCUS
Author(s): **ARTAVANISTSAKONAS S**; SIMPSON P
Corporate Source: YALE UNIV,HOWARD HUGHES MED INST,DEPT CELL BIOL/NEW HAVEN//CT/06520; YALE UNIV,HOWARD HUGHES MED INST,DEPT BIOL/NEW HAVEN//CT/06520; FAC MED STRASBOURG,INSERM,CNRS,UNITE BIOL MOLECGEN GENET 184,GENET MOLEC LAB/F-67085 STRASBOURG//FRANCE/
Journal: TRENDS IN GENETICS, 1991, V7, N11-1, P403-408
Language: ENGLISH Document Type: REVIEW
Abstract: During the development of Drosophila melanogaster, individual cells must make choices between a restricted set of possible fates in order to give rise to spatial patterns composed of different types of differentiated cells. The **Notch** locus appears to play a central and general role in the regulative events that control the local architecture of the final cellular pattern in several tissues, among